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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/060,188	04/14/1998	DOMINIC P. BEHAN	AREN-001CIP(001.US2.CIP)	9333

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BOZICEVIC, FIELD & FRANCIS LLP (AREN)
(ARENA PHARMACEUTICALS, INC.)
1900 UNIVERSITY AVENUE
SUITE 200
EAST PALO ALTO, CA 94303

EXAMINER	
HOWARD, ZACHARY C	
ART UNIT	**PAPER NUMBER**
1646	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/060,188	BEHAN ET AL.	
	Examiner	Art Unit	
	Zachary C. Howard	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34,40,45-66 and 69-74* is/are pending in the application.

4a) Of the above claim(s) *71-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34,40,45-66,69 and 70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *34,40,45-66 and 69-74* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 January 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 4/2/07 has been entered in full. Claims 45, 63-66, 69 and 70 are amended. Claims 67 and 68 are canceled. Claims 1-33, 35-39, 41-44, 75 and 76 were canceled previously. Claims 71-74 remain withdrawn as drawn to a non-elected invention as set forth in the 11/19/02 Office Action.

Claims 34, 40, 45-66, 69 and 70 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

The following page numbers refer to the previous Office Action (10/6/06).

The objections to the specification at pg 2 are *withdrawn* in view of Applicants' amendments to the title of the specification.

The potential objections to claims 65 and 66 as being duplicate claims (if claims 63 and 64 were to be found allowable) that were noted on pg 3 are rendered moot by Applicants' amendments to claims 65 and 66.

The objection to claim 66 at pg 4 is withdrawn in view of Applicants' amendments to the claim.

All rejections of claims 67 and 68 are moot in view of Applicants' cancellation of these claims.

The rejection of claims 63-66 under 35 U.S.C § 112, second paragraph, at pg 10 for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is *withdrawn* in view of Applicants' amendments to the claims.

Maintained Objections and/or Rejections

Claim Rejections - 35 USC § 101, utility

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 34, 40, 45-66, 69 and 70 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. This rejection was set forth at pg 4-7 of the 10/6/06 Office Action.

Applicants' arguments (4/2/07; pg 7-10) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response, Applicants argue that the "totality of the evidence demonstrates a specific, substantial and credible utility and that the Office has not provided evidence that it is more likely than not that Applicants' statement of utility are false" (pg 8). Applicants quote a statement from *In re Langer* (1974) stating that a disclosure of utility corresponding in scope to the claimed subject matter is sufficient to satisfy the utility requirement unless there is a reason for the skilled artisan to question the objective truth of the statement of utility or its scope.

Applicants' arguments have been fully considered but are not found persuasive. The rejection set forth previously provided a detailed explanation of why the claimed invention has no specific and substantial utility. This rejection is maintained for the reasons set forth previously and reiterated herein.

Applicants argue that the claimed methods are limited to orphan GPCRs that are associated with a disease or a disorder in a mammal. Applicants argue that it is incorrect to conclude that the claimed invention lacks a specific and substantial utility because the claims are not limited to a specific orphan GPCR associated with a specified disease or disorder in a mammal. Applicants argue that the claimed method can be applied to any orphan GPCR that meets the requirements of the claim (association with a disease or disorder). Applicants argue that the skilled artisan

practicing the claimed method would have in hand an orphan GPCR that has been associated with a disease or disorder. Applicants dispute that specification did not provide any examples of orphan GPCRs that were associated with a disease or disorder. Applicants point to two examples in the specification. Applicants first point to the GPR3, which is described in Example 4 and Figure 15 as being "more highly expressed in neuronal tissue from the temporal lobe of individuals with epilepsy as compared to individuals not suffering from this condition". Applicants next point to a constitutively active orphan GPCR associated with Kaposi's sarcoma. Applicants concede that a ligand was identified for this GPCR at the time of filing of the application (as disclosed in Gershengorn et al, January 1997; cited in previous Office Action at pg 9). However, Applicants argue that before the ligand was identified, this GPCR was an orphan this GPCR had been associated with a disease.

Applicants' arguments have been fully considered but are not found to be persuasive. The fact that the GPCR associated with Kaposi's sarcoma was once an orphan GPCR is not relevant to the utility of the claimed invention at the time of filing. As set forth at pg 8-9 of the 10/6/06 Office Action, at the time of filing of the instant application on 4/14/1997, the GPCR associated with Kaposi's sarcoma was not an orphan GPCR because Gershengorn et al (January 1997) had identified a ligand to said GPCR. Therefore, at the time of filing of the instant application, GPCR associated with Kaposi's sarcoma is not encompassed by the GPCRs to be used in the instant claims (i.e., orphan GPCRs associated with a disease or disorder). Therefore, the GPCR associated with Kaposi's sarcoma does not provide support for a utility for the claimed methods. With respect to GPR#, Applicants' results have been fully considered. In view of these results, Applicants' arguments are found persuasive that GPR3 was an example of an orphan GPCR associated with a disease (epilepsy) at the time of filing. However, a single example of a specific orphan GPCR (GPR3) that is reasonably correlated with a specific disease (epilepsy) does not provide a specific and substantial utility for an unspecified genus of orphan GPCRs that are associated with an unspecified genus of diseases or disorders. No reasonable correlation has been provided between a genus of orphan GPCRs and a specific disease or disorder.

Therefore, the claimed method of use of orphan GPCRs associated with a disease or disorder lacks a specific and substantial utility.

As set forth previously, Applicants' claims are directed to methods of screening using an endogenous GPCR that "has been associated with a disease or disorder" and "an endogenous ligand for said endogenous GPCR has not been identified" (claim 69 and dependent claims) or an endogenous constitutively active GPCR that "has been associated with a disease or disorder" and "an endogenous ligand for said endogenous GPCR has not been identified" (claim 70 and dependent claims). Each method of screening requires an orphan GPCR that has been associated with a disease or disorder. However, each claimed method lacks specific and substantial utility because the orphan GPCRs to be used are associated with an *unspecified* disease or disorder. As set forth in the Revised Interim Utility Guidelines Training Materials (available at www.uspto.gov/web/offices/pac/utility/utilityguide.pdf), a specific utility is "a utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. For example...a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent of a disclosure of what condition can be diagnosed" (pg 5-6). Furthermore, a substantial utility must be "a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities...the following are examples of situations that require or constitute carrying out further research to identify or confirm a "real world" context of use and, therefore, do not define "substantial utilities": A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved. B. A method of treating an unspecified disease or condition. C. A method of assaying for or identifying a material that itself has no "specific and/or substantial utility"..." (pg 6). In the instant case, the instant specification, as filed, provides a single example of an orphan GPCR (GPR3) that is associated with a disease (epilepsy) and does not provide any examples of constitutively active orphan GPCRs that were associated with a disease or disorder.

The association of a known orphan GPCR with a disease or disorder constitutes "carrying out further research to identify or confirm a "real world" context of use".

In the case *In re Fisher* (76 USPQ2d 1225 (CA FC 2005)) the U.S. Court of Appeals Federal Circuit stated, "Patent application does not satisfy utility requirement of 35 U.S.C. §101 unless it discloses both "substantial" utility for claimed invention, in form of significant and presently available benefit to public, as well as "specific" utility, which is well-defined and particular benefit to public" (pg 1225) and "an application must show that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research. Simply put, to satisfy the "substantial" utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public" (pg 1230).

In summary, the proposed uses of the claimed invention rely on orphan GPCRs that are associated with unspecified diseases or disorders, and that require further research to identify the nature of the specific diseases or disorders. Therefore, the instant application fails to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a specific or substantial utility.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34, 40, 45-66, 69 and 70 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention so that it would operate as intended without undue experimentation. This rejection was set forth at pg 7 of the 10/6/06 Office Action.

Applicants' arguments (4/2/07; pg 10) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response, Applicants submit that the rejection of the claims for lack of utility "has been adequately addressed in the discussion in the preceding section of this response" (i.e., Applicants' response to the rejection under 35 U.S.C. § 101 for lack of utility).

Applicants' arguments have been fully considered but are not found persuasive. For the reasons described above in the section "Claim Rejections – 35 USC § 101", the claimed invention is not supported by a specific and substantial asserted utility, and therefore it is maintained that one of skill would not know how to use the claimed invention without undue experimentation.

Claim Rejections - 35 USC § 112, 1st paragraph, written description

Claims 34, 40, 45-66, 69 and 70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection was set forth at pg 7-10 of the 10/6/06 Office Action.

Applicants' arguments (4/2/07; pg 11-12) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response, Applicants submit that the instant application as filed provides examples of orphan GPCRs that have been associated with a disease. Applicants point to two examples. First, Applicants submit that the specification "provides data showing that the orphan receptor GPR3 is more highly expressed in neuronal tissue from the temporal lobe of individuals with epilepsy as compared to individuals not suffering from this condition" (pg 75, lines 5-7; Figure 15). Second, Applicants submit that the specification describes a constitutively active orphan GPCR that has been associated with Kaposi's sarcoma (pg 65, lines 14-22). In response to the argument that this orphan GPCR had a ligand identified prior to filing of the instant application, Applicants argue that this orphan GPCR was associated with a disease prior to identifying the ligand.

Applicants' arguments have been fully considered but are not found persuasive. As set forth previously, *Vas-Cath Inc. v. Mahur*kar, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed" (pg 1117). As set forth at pg 8-9 of the 10/6/06 Office Action, at the time of filing of the instant application on 4/14/1997, the GPCR associated with Kaposi's sarcoma was not an orphan GPCR because Gershengorn et al (January 1997) had identified a ligand to said GPCR. The fact that it was once an orphan GPCR associated with a disease is not relevant because at the time of filing of the instant application, this GPCR is not encompassed by the genus of GPCRs to be used in the instant claims (i.e., orphan GPCRs associated with a disease or disorder). Therefore, the GPCR associated with Kaposi's sarcoma does not provide support for a written description of the claimed methods. With respect to GPR3, Applicants' results have been fully considered. In view of these results, Applicants' arguments are found to be persuasive that GPR3 was an example of an orphan GPCR associated with a disease (epilepsy) at the time of filing. However, a single example of a orphan GPCR (GPR3) that is associated with a specific disease (epilepsy) does not provide a description of a genus of orphan GPCRs that are associated with diseases or disorders. The description of GPR3 associated with epilepsy provides no description of other orphan GPCRs that are associated with diseases.

Applicants further note "that withdrawal of this rejection would be consistent with recent decisions by the Board of Patent Appeals and Interferences of the United States Patent and Trademark Office, such as *Ex parte Bandman* BPAI Appeal No. 2004-2319 (2004) and *Ex parte Sun* BPAI Appeal No. 2003-1993 (2003), among others. The genus claims that are the subject of these decisions were supported by disclosure of a *single* representative species encompassed by the claims. The instant application provides both a general description as well as specific examples of orphan GPCRs that are encompassed by the claimed inventions. As such, the Applicants submit that the instant

application at a minimum meets the criteria set forth in the above-referenced BPAI decisions" (pg 11-12).

Applicants' arguments have been fully considered but are not found persuasive. The Examiner does not dispute that disclosure of a single representative species encompassed by the claims *may* support claims to a genus. However, the specific BPAI decisions cited by Applicants (*Ex parte Bandman; Ex parte Sun*) are based on cases with significantly different fact patterns from the instant application and the decisions are not binding. In *Bandman*, the claimed invention encompassed a genus of polynucleotides of SEQ ID NO: 2 (1334 nucleotides); naturally-occurring variants of SEQ ID NO: 2 that are at least 95% identical; polynucleotides encoding a polypeptide of SEQ ID NO: 1 (338 amino acids); and polynucleotides encoding naturally-occurring variants of SEQ ID NO: 1 that are at least 95% identical. In *Sun*, the claimed invention encompassed an isolated polynucleotide of SEQ ID NO: 1; polynucleotides encoding a polypeptide of SEQ ID NO: 2; and polynucleotides having at least 80% identity to the coding region of SEQ ID NO: 1. In each of these applications, the claimed subject matter was related to nucleic acids encoding variants of a single "parent" amino acid sequence. In each case, the amino acid sequence of the encoded "parent" protein provides information as to which of the claimed variants may retain the functionality of the parent sequence. In contrast, in the instant application the claims recite a method of using a genus of orphan GPCRs (each of which has a different sequence of amino acids) that have been associated with a disease or disorder. In the instant case, the structure of the orphan GPCR provides no description of an associated disease or disorder. Furthermore, the description of a single orphan GPCR that is associated with a specific disease or disorder provides no description of the disease or disorder associated with other orphan GPCRs.

As set forth previously, each genus of GPCR (required to practice the method of the claims) recited in the claims lacks written description. The methods require an endogenous GPCR "wherein said endogenous GPCR has been associated with a disease" and "an endogenous ligand for said endogenous GPCR has not been identified". That is, the methods require an orphan GPCR that has been associated with

a disease. However, the specification as originally filed describes a single orphan GPCR that meets the description of the GPCR required by claim 69 (and dependent claims). The specification as originally filed does describe description of any endogenously constitutively active GPCRs as required by claim 70 (and dependent claims).

The written description requirement for a genus required for a claimed method may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information of any orphan GPCRs that are associated with a disease or disorder. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicants were not in possession of the claimed genus.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Therefore, the claims do not meet the written description provision of 35 U.S.C. §112, first paragraph. Applicants are reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (pg 1115).

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646